SOME OBSERVATIONS OF THE DIURNAL VARIATIONS IN LEUCOCYTE COUNT IN MAN, with SPECIAL REFERENCE TO THE EFFECT OF DIGESTION.

Being a record of 37 experiments.

by

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AS A THESIS FOR THE DEGREE

of

DOCTOR OF MEDICINE.

MARCH 1933.

C O N T E N T S

I N T R O D U C T I O N.

The problem of leucocytosis is an interesting and important one. Its great significance in pathological conditions renders the knowledge of the variations of the white blood cells under normal physiological conditions necessary, for without this knowledge our interpretation of the result of a leucocyte count does not rest on a sound basis and may be erroneous. Although some aspects of physiological increase in the number of white cells have been studied and settled, there seems to be much less definite agreement regarding the effect of food on the number of leucocytes in the peripheral blood of man. The literature bearing on the subject is enormous, and the results recorded are often contradictory in one or more points. When such a state of confusion exists, one is naturally at a loss as to what to believe. To secure peace of mind, and to add one more evidence, either in favour of or against one or the other theory, more observations do not seem to be altogether uncalled for.

SUMMARY OF LITERATURE.

Owing to the vast amount of literature on this subject, only historical landmarks and representative works which have direct bearing on the present investigation will be referred to. Arneth and Ostendorff [1], supporters of digestion leucocytosis, mention Nasse (1850) and Moleschott (1854) as the first to describe an increase in the number of white blood cells after meal. Hirt [2] in 1856, and later Pohl [3] in 1889, who made use of the Thoma Zeiss counting method newly introduced and who experimented on animals, both confirmed the findings of Nasse and Moleschott. Among many other observers further quoted by Arneth and Ostendorff [1] may be mentioned V. Limbeck and Reinert; V. Limbeck (1889), making observations after a meal of meat which was preceded by a preliminary fasting period of eighteen hours, found leucocytosis occurring one to six hours afterwards, but was convinced that it does not occur in every, and not always in the same individual; Reinert (1891) carried out experiments on himself for seven days and found an average increase of about 3000 cells, being highest four hours after mid-day meal, which he took at 11.30 a.m., but he could not observe any essential variation after breakfast or evening meal. Rieder [4], in 1892, made hourly examination on a number of children and adults after a meal rich in protein; out of a total of thirtyfive cases only twentysix exhibited post-prandial rise, which began soon after meal and reached the peak two to seven hours afterwards, the increase averaging 33% in adults. Goodall, Gulland, and Paton [5], in 1903, observed leucocytosis after food both in normal and splenectomised dogs which were previously fasted; they noted that a slight preliminary fall may occur, and then a fairly regular rise follows and reaches the maximum in about four hours after meal time. Rothacker [6], in 1919, concluded that in man the digestion leucocytosis is not a regular phenomenon, nor is it always of the same degree in the same individual, and that nature of food does not matter. Sirensky [7], however, found that carbohydrate and protein food causes greater leucocyte increase than fat and mixed food, but he also noted that the interval between food and the highest count varies greatly.

The chief points in connection with the supporters of digestion leucocytosis in man may be summed up as follows:-

(1) They maintain that the rise in the number of leucocytes occurs from one to seven hours after food, that the rise varies in different individuals, and that even in the same individual the time and extent of the leucocytosis are not always the same.

(2) The time of the day when food is given is often not mentioned, but when it is stated, the rise usually occurs in the afternoon.

(3) Practically all of them admit that some of the cases, including normal healthy subjects, do not exhibit the phenomenon of post-prandial leucocytosis.

(4) They did not appear to have controlled their results by making similar observations on fasting persons throughout the same period.

Grancher (1876), according to Rieder [4], was probably the first to make known that variations of the number of leucocytes occur independent of food. In 1900 Japha [8] made repeated observations on himself and came to the same conclusion, with the addition that the rise reaches its maximum in the afternoon and declines again towards the evening, while he failed to find evidence of digestion leucocytosis in sucklings under normal feeding. Türk (1912), quoted by Arneth and Ostendorff [1], also observed a similar rise and fall independent of food.

In 1925 Sabin [9] and co-workers were the first to make a complete investigation into the problem of physiological variations in the number of leucocytes. Blood was examined every fifteen minutes from 9 a.m. till 5 p.m. and the following conclusions were arrived at:-

(1) There is a characteristic rhythm of total white blood cells at intervals of approximately one hour duration.

(2) Total number of white blood cells varies in proportion of 1 to 2.

(3) The increase occurs in the afternoon regardless of food, the total increase being due to increase in neutrophils.

(4) The neutrophils die off in showers, often of considerable proportion. They are promptly replaced, and this replacement is responsible for the rhythmic variation.

After Sabin the credit for making the most extensive investigation into the same problem must be given to Shaw[10]. He found that

(1) during a 24 hour day total leucocytes of man exhibit two tides each occupying approximately 12 hours. The day tide begins in the forenoon (10a.m. - 1p.m.), reaches its flood during the afternoon, and completes its ebb in the evening. The night tide starts in the evening (9-11p.m.), attains its height in the hours after midnight, and ebbs away in the early forenoon.

(2) The tidal waves are the summation of rapid oscillations in the number of leucocytes occurring at intervals of about 15 minutes.

(3) The day and night tides occur regardless of food, exercise, and sleep.

(4) The curve of body temperature does not correspond with tidal curves.

Smith and Mc.Dowell[11] agree with Sabin in most respects, with the addition that the height of the number of leucocytes may be reached in the forenoon, though usually in the early afternoon, and that there appears to be an approximate pattern of variations for each person.

Garrey[12] also believes that food has no effect on the white count whatsoever, and thinks that rest reduces the number of the leucocytes to a minimum. Raisky[13], partly repeating Garrey's work, failed to observe any leucocytosis three hours after meal in four healthy students at rest and previously fasted, but found that there is a definite rise in the number of leucocytes after a continuous muscular exercise.

Ponder[14] and co-workers, examining the blood every forty-five minutes from 10.0 a.m. till 4.0 p.m. in persons under condition of moderate activity, have not observed the large fluctuations described by Sabin, and believe that the large fluctuations are due to errors of method. Employing his own technique and by counting 800 cells, Ponder found that the fluctuations do not exceed ±8% throughout the period of observation in his series of cases. He concluded that the fluctuations have no definite periodicity, and that the increase in the number of leucocytes in the afternoon is frequent but not constant.

Martin[15] observed afternoon rise in hospital convalescents; he is inclined, however, to attribute this to slight physical activity due to the making of bed and to patients sitting up in bed and washing themselves. Pursuing his investigations further, with a view to testing the efficacy of Widal's Haemoclasic Crisis Test, he concluded, in the following paper, that variations of leucocytes following ingestion of full meal, milk, peptone, in both normal subjects and patients with hepatic diseases, fall within the normal range of variations in fasting subjects.

SOURCE AND NATURE OF INCREASED LEUCOCYTES.

Goodall and Paton[16] found in animal experiments that the source of increased cells is the bone marrow, and that the rise in lymphocytes is constant both in incidence and degree, although in a minority of cases, the polymorphs may show a considerable rise. Sabin[9] did not arrive at any definite conclusion as to the source of the increased neutrophils. Shaw[10] found that the curve of the neutrophils follows the tidal curve closely, while the lymphocyte curve does not. Smith and Mc.Dowell[11], however, noted that the total lymphocytes and the total neutrophils both correspond with the tidal curve in its rise and fall, but, the total increase in the number of lymphocytes being small, the total lymphocyte curve is not greatly affected, Ponder[14] found the neutrophils mostly responsible for the increase, and concluded that the variations and fluctuations are due to redistribution. Martin[15] found that the afternoon rise is due to increase of all cell types, but more especially the lymphocytes. Results of qualitative changes recorded in earlier literature by supporters of digestion leucocytosis are also not unanimous.

The basophils and eosinophils, according to most authors, do not show any great or constant change.

PURPOSE OF IN INVESTIGATION.

(1) To make observations on leucocytic variations in normal fasting persons.

(2) To test the effect of meal on the number of leucocytes in man after a preliminary fasting period.

(3) To investigate variations in the white cell count in pathological cases without fasting of any kind.

TECHNIQUE FOR BLOOD EXAMINATION.

Method of obtaining blood:

Blood is obtained from near the tip of the finger. The part is rubbed with cotton wool soaked in ether, and, when dried, is pricked to a depth of about 3 m.m. with an automatic lancet with a blade of about 2m.m. broad at its widest part. The first drop of the spontaneously oozing blood is discarded, and only subsequent drops are used for the purpose of examination, a fresh drop being employed each time for the white count, differential count, and for haemoglobin estimation. The blood thus obtained is believed to be a mixture of arterial and venous capillary blood.

Leucocyte Count:

Thoma Zeiss white pipette and Bürker-Türk double counting chamber are used, the same set being used throughout each experiment. A dilution of 1 in 20 is made with the usual white diluting fluid (1% glacial acetic acid in aq. dest. coloured with methyl green). The content of the pipette is thoroughly shaken and rotated continuously for at least 3 minutes. The first two big drops from the pipette are discarded, and the next drop is run into one side of the chamber by capillary action. Two more drops are blown away, and then another drop of suitable size is similarly introduced into the other half of the counting chamber for control count. All the cells lying within the ruled area (9 sq.m.m.) in each half of the chamber are counted, and the average is taken from the entire count, which varies from 500-1000 cells.

Differential Count:

Films are made on 7/8 in. square coverslips and stained by the Jenner-Giemsa method. A count of 300-500 white cells is made from each pair of cover-slips, equal number being counted from each slip. A lymphocyte count includes both large and small lymphocytes and large mononuclears or 'transitionals'.

Haemoglobin Estimation:

Haemoglobin is estimated at intervals to exclude the possibility of the increase in the number of leucocytes being due to concentration of the blood. Sahli's Haemoglobinometer is employed.

Care of Instruments.

Special care is taken that the instruments are absolutely clean and dry before each use.

Experimental Errors:

In spite of all the above precautions it is not possible to get an absolutely uniform distribution of the cells in the counting chamber and probably also a perfectly homogeneous mixture in the mixing chamber. However, the errors are minimised by counting a large number of cells as outlined above.

It has been found, throughout the whole work, that the difference between the two halves of the counting chamber is practically always between nil and 600 cells per c.mm. of undiluted blood. The error is further reduced by taking the average of both counts.

EXPRESSION OF RESULTS.

The results are expressed in tabular and graphic forms. The abbreviations used are as follows:-

B = Basophil Polymorphs.

E = Eosinophil "

N = Neutrophil "

L = Lymphocytes (including large mononuclears).

On the graph:

The curve represents the total number of the leucocytes per c.mm. The absolute numbers of the neutrophil polymorphs and lymphocytes are approximately represented by black and red vertical lines placed just about opposite the times when the Differential Counts are made. Meal time is indicated by a bold vertical arrow.

GROUP I.

OBSERVATIONS ON FASTING PERSONS.

Conditions of experiment:

All subjects are normal healthy adults who fast from 7.0 - 9.0p.m. the previous evening till 3.0p.m. next afternoon. Blood count is made hourly from 10.0a.m. till 3.0 p.m. Although the primary object of this series of experiments is to observe variations during fasting period, it is thought that it might be advantageous to test the effect of food given late in the afternoon at the end of the fasting experiment. A full mixed meal, consisting of meat, potatoes, vegetables, bread, butter, pudding, and a cup of tea, is given at 3.30p.m., and one more white count is made two hours afterwards in most of the cases. From half an hour before till the end of the experiment, physical rest is enjoined, the subjects sitting comfortably in an armchair, and being allowed up only for a few minutes after each sample of blood has been taken. As it is practically impossible to obtain a state of absolute mental rest during the waking hours, magazine reading is allowed.

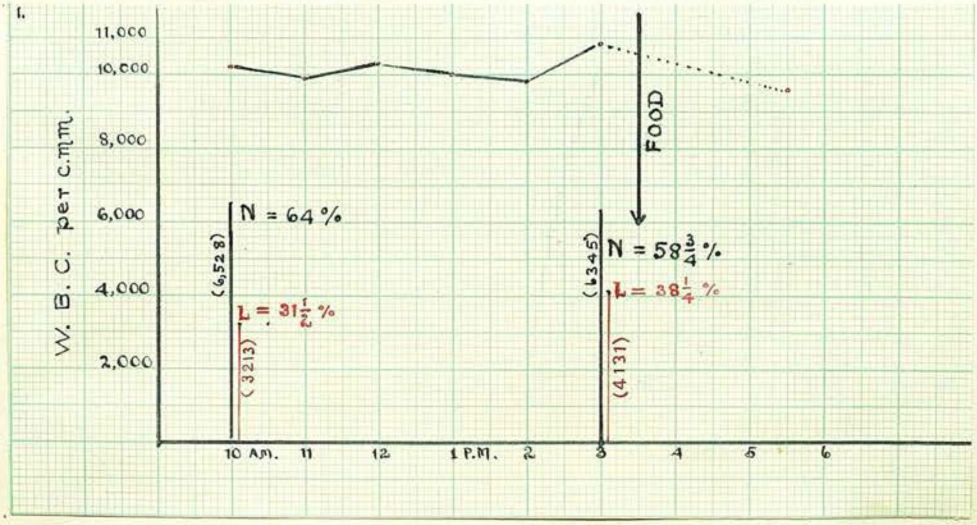
Experiment 1.

Z., male, aet. 24 years, healthy student.

Last meal: 8 p.m. previous evening.

TABLE OF RESULTS.

Time.	w.b.c. per c.m.m.	Differential Count.
10.0 a.m.	Hb. 100% 10,200	B= $1\frac{1}{4}$%; E= $3\frac{1}{4}$%; N= 64%; L= $31\frac{1}{2}$% (127) (331) (6528) (3213)
11.0	9,900	
12.0	10,300	
1.0 p.m.	10,000	
2.0	9,800	
3.0	Hb. 100% 10,800	B= $\frac{3}{4}$%; E= $2\frac{1}{4}$%; N= $58\frac{3}{4}$%; L= $38\frac{1}{4}$% (81) (243) (6345) (4131)
3.30	Full Meal.	
5.30	9,600	



Remarks:-

Fasting Period: Lowest count at 2.0p.m. = 9,800per cmm

Highest " " 3.0p.m. = 10,800 " "

Difference = 1,000 cells = 12.5% " "

2 hours after meal = no increase.

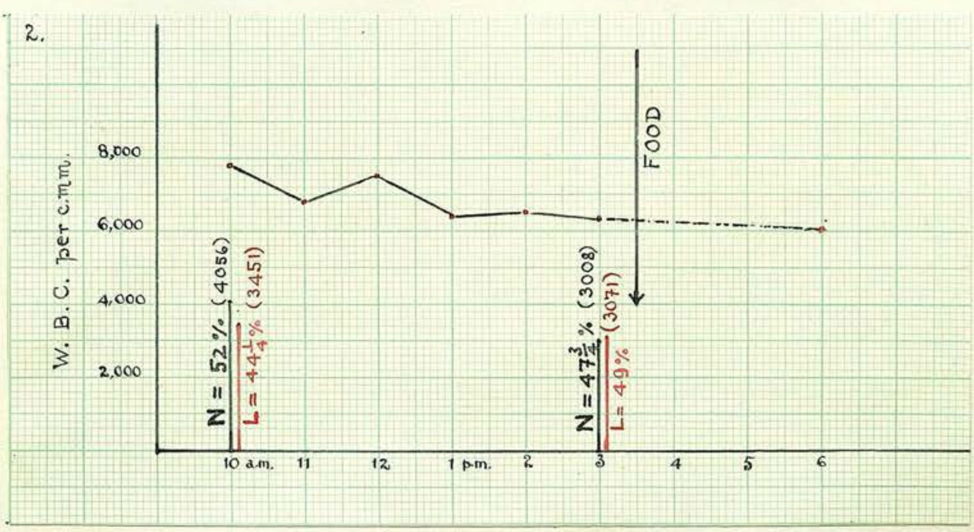
Experiment 2.

J.B., male, aet.21 years, healthy.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	w.b.c.	Differential Count.
10.0 a.m.	Hb.100% / 7,800	B=$\frac{1}{4}$%; E=3$\frac{1}{2}$%; N=52%; L=44$\frac{1}{4}$% (19) (273) (4056) (3451)
11.0	6,800	
12.0	7,500	
1.0 p.m.	Hb.100% / 6,400	
2.0	6,500	
3.0	Hb.100% / 6,300	B=$\frac{1}{2}$%; E=2$\frac{3}{4}$%; N=47$\frac{3}{4}$%; L=49% (31) (173) (3008) (3071)
3.30	Full meal.	
6.0	6,000	



Remarks:-

Fasting blood: Lowest count at 3.0 p.m. = 6,300

Highest 10.0 a.m. = 7,800

Difference = 1,500 cells = 23.8%

2$\frac{1}{2}$ hours after meal = no increase.

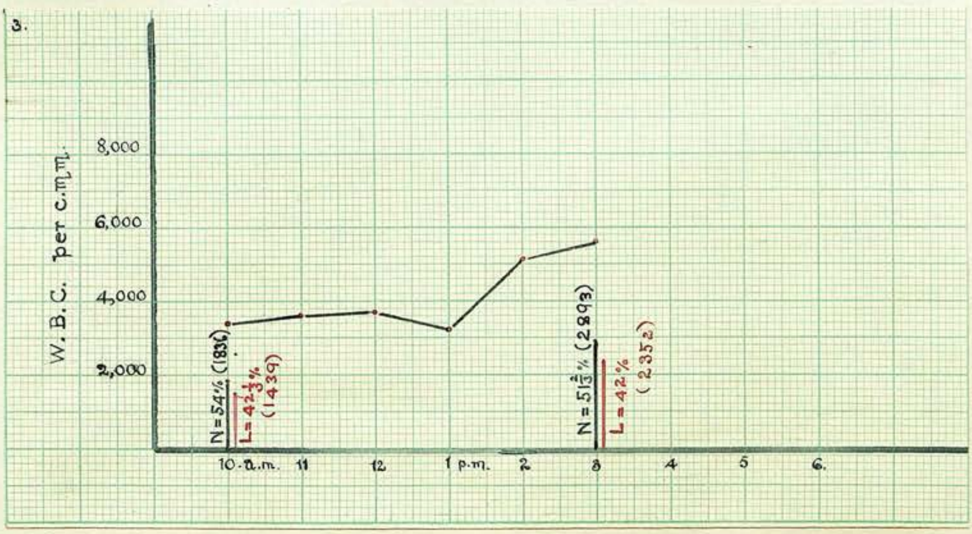
Experiment 3.

A.K., male aet 34 years, healthy.

Last meal: 7.30 p.m. previous evening.

TABLE OF RESULTS.

Time	W.b.c.	Differential Count.
10.0 a.m.	Hb.98% 3,400	B=0.3%; E=3.3%; N=54%; L=42.3% (11) (113) (1836) (1439)
11.0	3,600	
12.0	3,700	
1.0 p.m.	3,200	
2.0	5,100	
3.0	Hb.99% 5,600	B=0.3%; E=6%; N=51.6%; L=42%. (19) (336) (2893) (2352).



Remarks:

Fasting blood: Lowest count at 1.0 p.m. = 3,200

Highest 3.0 p.m. = 5,600

Difference = 2,400 cells = 75%.

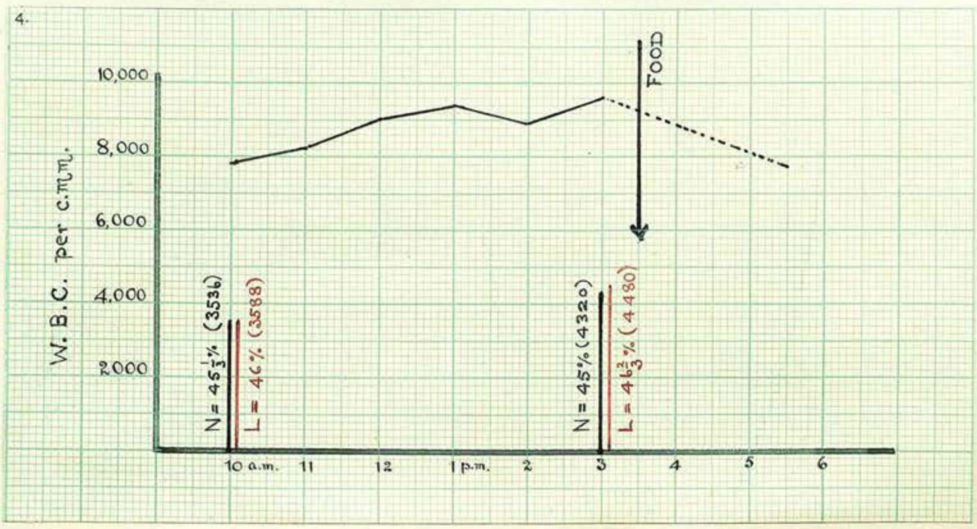
Experiment 4.

D., male aet. 30 years, healthy.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time	W.B.C.	Differential Count.
10.0 a.m.	Hb. 102% 7,800	B=1%; E=7.6%; N=45.3%; L=46% (78) (598) (3536) (3588)
11.0	8,200	
12.0	9,000	
1.0 p.m.	Hb. 102% 9,400	
2.0	8,900	
3.0	Hb. 102% 9,600	B=1.3%; E=7%; N=45%; L=46.6% (128) (672) (4320) (4480)
3.30	Full meal.	
5.30	7,700	



Remarks:

Fasting blood: Lowest count at 10.0 a.m. = 7,800

Highest 3.0 p.m. = 9,600

Difference = 1,800 cells = 23%

2 hours after meal = no increase.

Experiment 5.

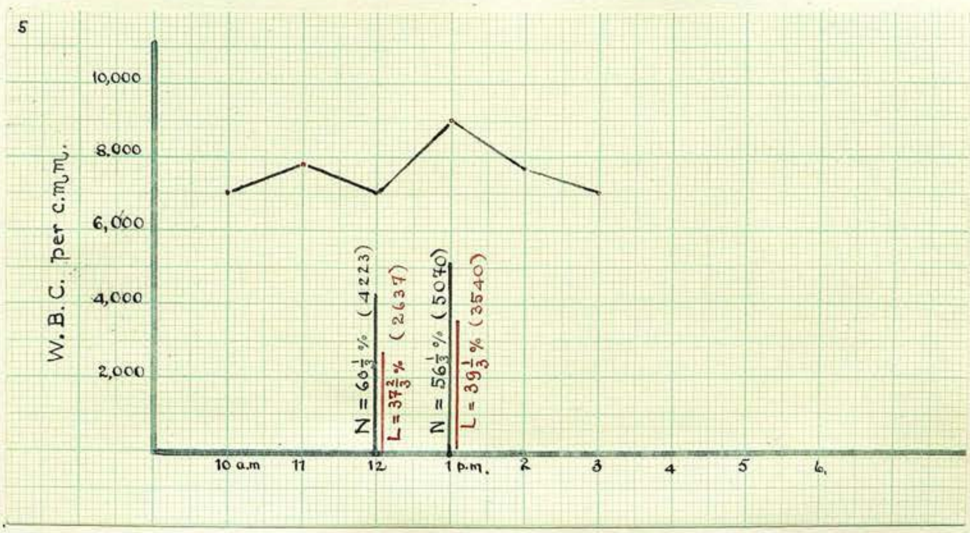
Mrs. C., aet. 35 years, a healthy blood donor.

Has given 8 pints within the last 18 months, the last being 4 days ago.

Last meal: 8.0 p.m. previous evening.

TABLE OF RESULTS

Time	w.b.c.	Differential Count.			
10.0 a.m.	Hb. 50% 7,000				
11.0	7,800				
12.0	Hb. 50% 7,000	B= 0.6%; (47)	E= 1.3%; (93)	N= 60.3%; (4223)	L= 37.6% (2637)
1.0 p.m.	Hb. 50% 9,000	B= 1.3%; (120)	E= 3%; (270)	N= 56.3%; (5070)	L= 39.3% (3540)
2.0	Hb. 50% 7,700				
3.0	7,000				



Remarks:

Fasting blood: Lowest count at 10.0 a.m. = 7,000
Highest 1.0 p.m. = 9,000
Difference = 2,000 cells = 28.6%.

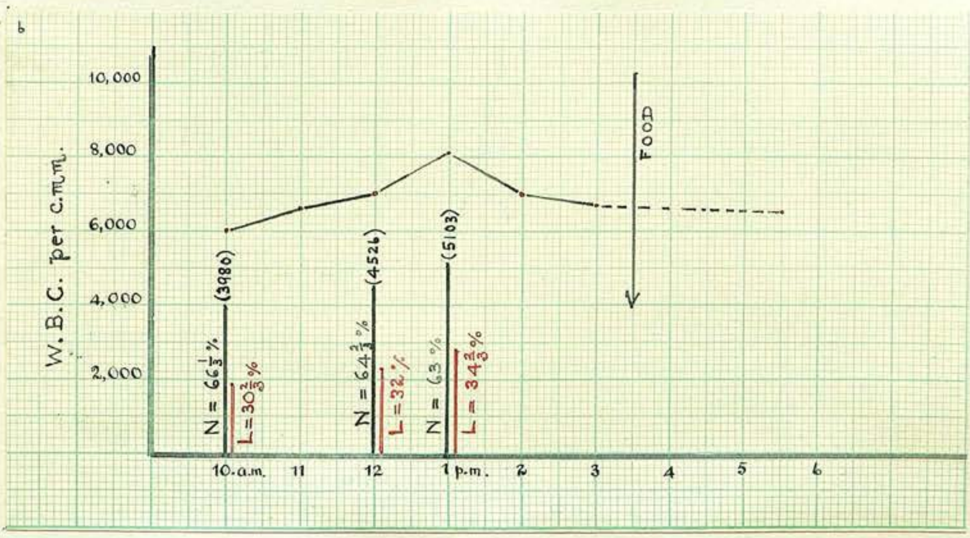
Experiment 6.

C., male aet 48 years, healthy.

Last meal: 8.0 p.m. previous evening.

TABLE OF RESULTS.

Time	W.b.c.	Differential Count.
10.0 a.m.	Hb. 99% 6,000	B=0.3%; E=2.6%; N=66.3%; L=30.6% (20) (160) (3980) (1840)
11.0	6,600	
12.0	7,000	B=0.3%; E=3%; N=64.6%; L=32%. (23) (210) (4526) (2240)
1.0 p.m.	Hb. 100% 8,100	B=0.3%; E=2%; N=63%; L=34.6%; (27) (162) (5103) (2808)
2.0	7,000	
3.0	Hb. 100% 6,700	
3.30	Full meal.	
5.30	6,500	



Remarks:

Fasting blood: Lowest count at 10.0 a.m. = 6,000
Highest 1.0 p.m. = 8,100
Difference = 2,100 cells = 35%.
2 hours after meal = no increase.

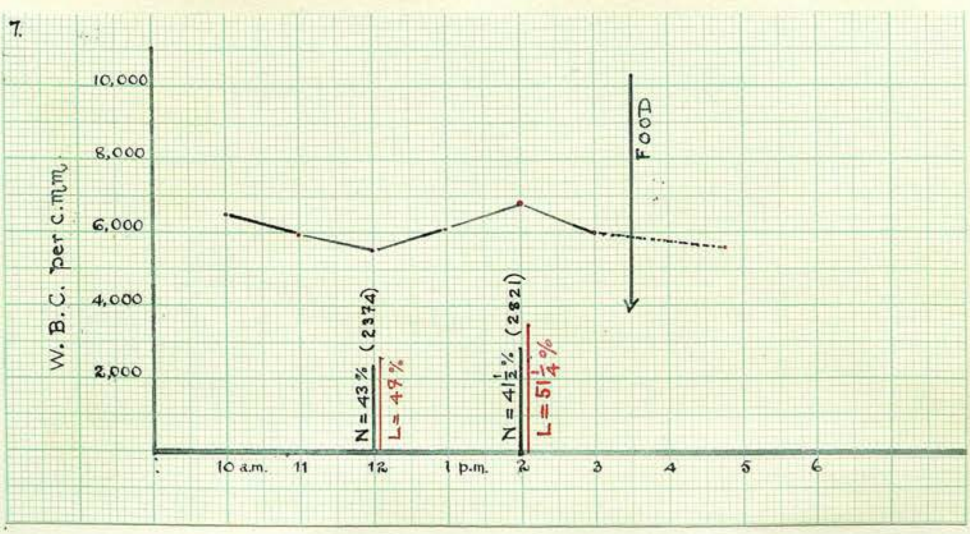
Experiment 7.

S.V., male aet. 25 years, healthy student.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time	W.b.c.	Differential Count.
10.0 a.m.	6,500	
11.0	Hb.101% 5,920.	
12.0	5,520	B= 0%; E= 10%; N= 43%; L= 47%. (0) (552) (2374) (2595).
1.0 p.m.	Hb.101% 6,040	
2.0	Hb.101% 6,800	B= ¼%; E= 7%; N= 41½%; L= 51¼%. (17) (476) (2822) (3485).
3.0	6,000	
3.30	Full meal.	
4.45	5,600	



Remarks:

Fasting blood: Lowest count at 12.0 a.m. = 5,520
Highest 2.0 p.m. = 6,800
Difference = 1280 cells = 23.2%
1¼ hours after meal = no increase.

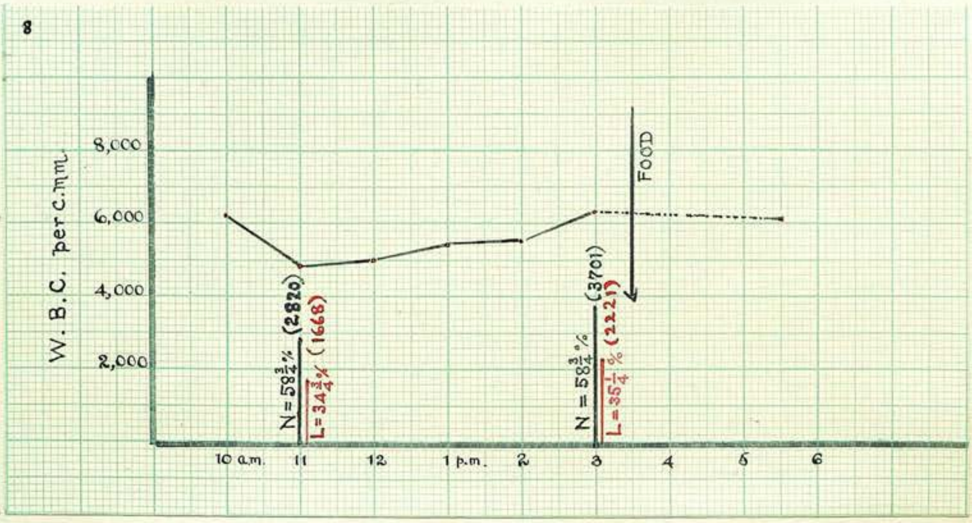
Experiment 8.

O., male aet. 24 years, healthy student.

Last meal: 9.0 p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c.	Differential Count.
10.0 a.m.	Hb. 100% / 6,200	
11.0	4,800	B= 0%; E= $6\frac{1}{2}$%; N= $58\frac{3}{4}$%; L= $34\frac{3}{4}$% (0) (312) (2820) (1668).
12.0	5,000	
1.0 p.m.	5,400	
2.0	Hb. 100% / 5,500	
3.0	Hb. 100% / 6,300	B= $\frac{1}{4}$%; E= $5\frac{3}{4}$%; N= $58\frac{3}{4}$%; L= $35\frac{1}{4}$%. (16) (362) (3701) (2221)
3.30	Full meal.	
5.30	6,100	



Remarks:

Fasting blood: Lowest count at 11.0 a.m. = 4800
Highest 3.0 p.m. = 6300
Difference = 1500 cells = 31.2%
2 hours after meal = no increase.

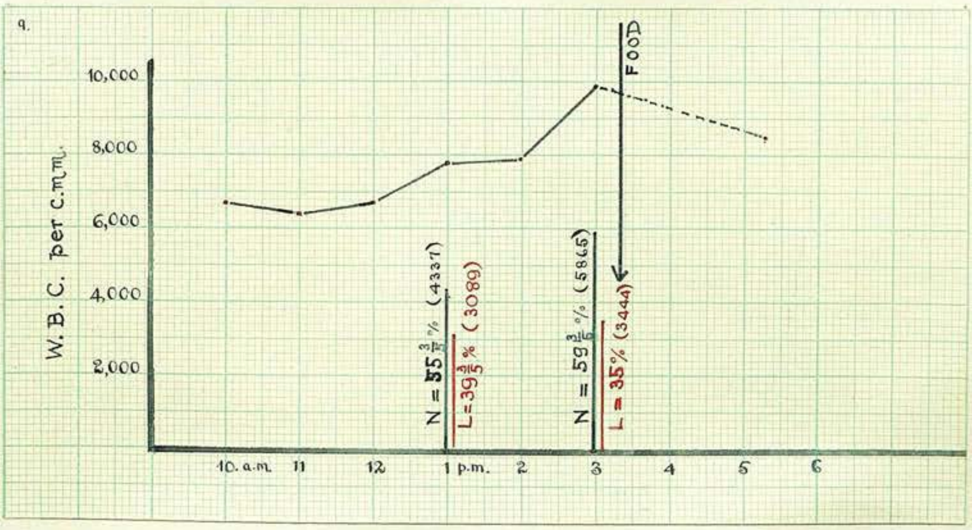
Experiment 9.

J.Y., male aet. 26 years, healthy.

Last meal: 8.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	W.b.c.	Differential Count.
10.0 a.m.	Hb.100% 6,700	
11.0	6,400	
12.0	6,700	
1.0 p.m.	Hb.100% 7,800	B=0.6%; E=4.2%; N=55.6%; L=39.6% (47) (328) (4337) (3089)
2.0	7,850	
3.0	Hb.100% 9,840	B=0.8%; E=4.6%; N=59.6%; L=35% (79) (453) (5865) (3444)
3.20	Full meal.	
5.20	8,460.	



Remarks:

Fasting blood: Lowest count at 11.0 a.m. = 6,400.
Highest 3.0 p.m. = 9,840
Difference = 3,400 cells = 54%
2 hours after meal = no increase.

G R O U P I.

TABLE OF COMPARISON.

No. of Expt.	Lowest Count per c.mm.	Time.	Highest Count per c.mm.	Time.	Difference	Results of Meal given 3.30 p.m.
1	9,800	2p.m.	10,800	2p.m.	1000=12.5%	Decrease 2 hours after
2	6,300	3p.m.	7,800	10a.m.	1500=23.8%	Decrease 2 hours after
3	3,200	1p.m.	5,600	3p.m.	2400=75%	-
4	7,800	10a.m.	9,600	3p.m.	1800=23%	Decrease 2 hours after
5	7,000	10a.m.	9,000	1p.m.	2000=28.6%	-
6	6,000	10a.m.	8,100	1p.m.	2100=35%	Decrease 2 hours after
7	5,520	12a.m.	6,800	2p.m.	1280=23.2%	Decrease $1\frac{1}{4}$ hours after
8	4,800	11a.m.	6,300	3p.m.	1500=31.2%	Decrease 2 hours after
9	6,400	11a.m.	9,840	3p.m.	3440=54%	Decrease 2 hours after

SUMMARY.

(1) Hourly leucocyte count is made from 10 a.m. till 3 p.m. on 9 fasting healthy adults sitting quietly and comfortably.

(2) 8 cases show an afternoon rise, beginning in the late forenoon or early afternoon. A big meal is given at 3.30 p.m., and in 5 cases a white count is made 2 hours, in 1 case 2½ hours, and in another case 1¼ hours, after the meal. In all the cases the leucocyte count made after the meal is lower than the one made preceding the meal. The peak of the rise has been reached before the post-prandial count is made, and is then followed by a fall, which is not influenced by digestion.

(3) The absolute numbers of both the neutrophil polymorphs and the lymphocytes practically always follow the rise and fall of the total leucocytes, except in Expt. (1), in which the increase is due to lymphocytes alone. The relative percentage either remains practically the same or shows a small alteration in either direction up to about 7%, with an average of approximately 3% for both neutrophils and lymphocytes.

(4) Changes in the numbers of basophils and eosino-

phils are variable and generally small, the maximum alteration observed being an increase of 223 eosinophils per c.mm. or 2.7%.

(5) Taking the lowest count as 100%, the maximum variation observed between 10 a.m. and 3 p.m. ranges from 12.5% to 75%, with an average of 34%.

(6) Although the lowest count usually occurs in the forenoon, it may occur in the early afternoon shortly before the rise begins.

(7) Apart from a definite rise or fall, the total number of leucocytes may exhibit fluctuations of about ±500-1000 cells per c.mm., but by the hourly counting procedure no definite regularity has been observed.

(8) The haemoglobin percentage remains practically constant throughout, and therefore the increase in leucocytes is not due to blood concentration.

(9) Some deviations from average count for normal persons are noted in this group of apparently healthy subjects, viz.

Lowest count seen = 3,200 W.B.C. per c.mm.
Highest " " = 10,800 " " "
Neutrophil polymorphs as low as 41½%.
Lymphocytes as high as 51%.
Basophils " " " 1.3%.

Eosinophils in 5 out of 6 students from the tropics are above 4%, the highest being 10% in one count.

G R O U P II.

A. EFFECT OF MID-DAY MEAL AFTER A FAST

Conditions of experiment:

In this series meal is given between 12.30-1.0p.m., i.e. after a fasting period of about 18 hours. Three hourly counts are made from 10.0 to 12.0a.m., in order to have a good idea of the level of the number of the leucocytes in the morning, followed by three or more hourly examinations after meal in the afternoon. Three subjects are healthy volunteers (two of which have already appeared in GROUP I. Expt. 1 and 9), while the rest are hospital patients whose general health at the time of the experiment is, however, quite satisfactory. The healthy volunteers are subject to the general conditions laid down in GROUP I., while the hospital patients stay in bed during the period of observation.

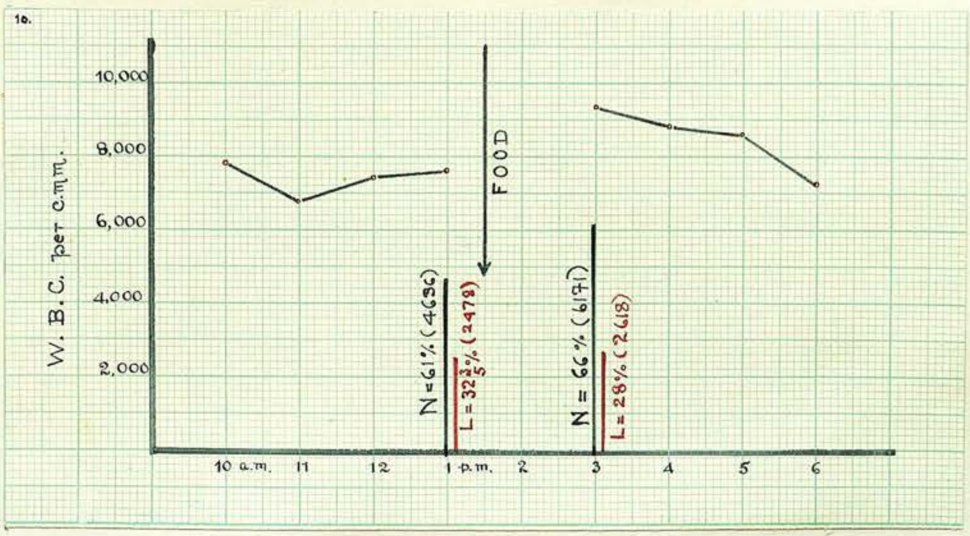
Experiment 10.

J.Y., male aet.26 years, healthy.
(same subject as in Expt. 9)
Interval between the two experiments = 2 months.

Last meal: 7.0p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.100% 7,800	
11.0	6,750	
12.0	7,400	
1.0 p.m.	Hb.100% 7,600	B=0.4%; E=6%; N=61%; L=32.6% (30) (456) (4636) (2478)
1.30	Full meal.	
3.0	Hb.100% 9,350	B=0.4%; E=5.6%; N=66%; L=28% (37) (524) (6171) (2618)
4.0	8,800	
5.0	8,600	
6.0	7,200	



Remarks: Lowest count at 11.0 a.m. = 6,750 per cmm.
Highest " " 3.0 p.m. = 9,350 " "
Difference = 2,600 cells = 38.5% " "
Results are essentially the same as in Expt. 9. Meal and experimental conditions are practically identical in both experiments.

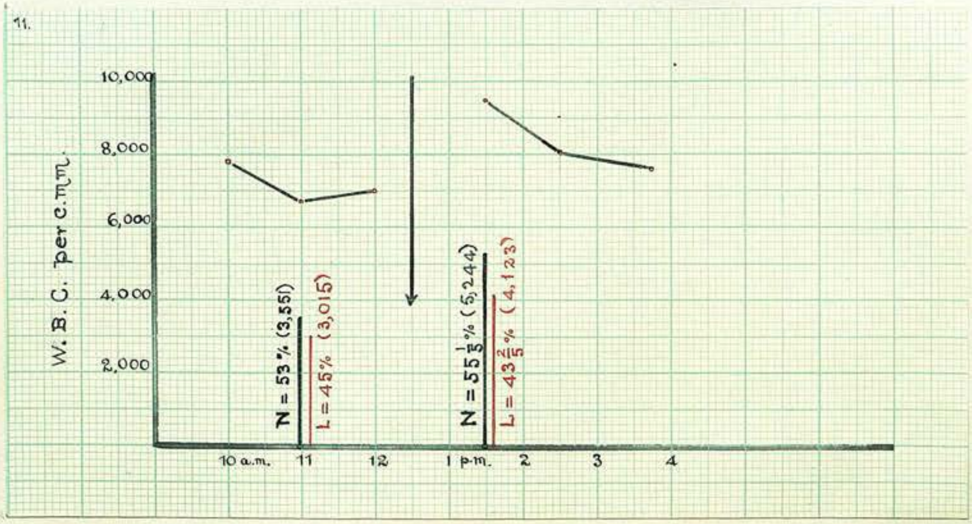
Experiment 11.

Mrs. C., aet. 35 years, healthy blood donor.
(same subject as in Expt. 5, but about two months afterwards).

Last meal: 9.0 p.m. previous evening.

TABLE OF RESULTS

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.76% 7,800	
11.0	6,700	B=0.2%; E=1.8%; N=53%; L=45% (13) (120) (3551)(3015)
12.0	7,000	
12.30	Full meal.	
1.30 p.m.	Hb.75% 9,500	B=0.2%; E=1.2%; N=55.2%; L=43.4% (19) (114) (5244) (4123)
2.30	8,100	
3.45	7,600	



Remarks:

Lowest count at 11.0 a.m. = 6,700 per c.mm.
Highest " " 1.30p.m. = 9,500 " "
Difference = 2,800 cells = 41.8%
Results are similar to those in Expt. 5.
Conditions of experiment and nature of meal are similar in both experiments.

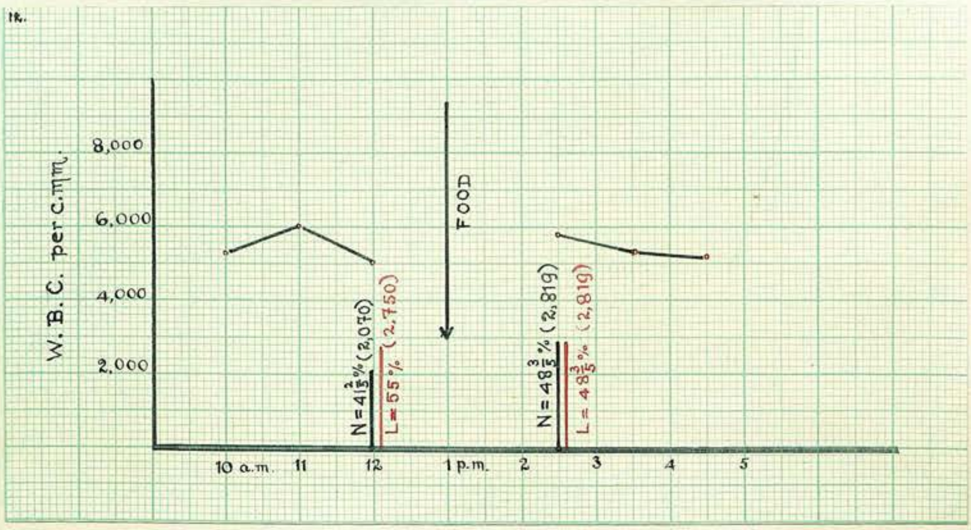
Experiment 12.

Miss J.M., aet. 39 years, healthy.

Last meal: 8.0 p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.100% 5,300	
11.0	6,000	
12.0	Hb.100% 5,000	B=0.4%; E=3.2%; N=41.4%; L=55% (20) (160) (2070) (2750)
1.0 p.m.	Full meal.	
2.0	Hb.100% 5,800	B=0.4%; E=2.4%; N=48.6%; L=48.6% (23) (139) (2819) (2819)
3.0	5,300	
4.0	Hb.100% 5,200	



Remarks:

Lowest count at 12.0 a.m. = 5,000 per c.mm.
Highest " " 11.0 a.m. = 6,000 " "
Difference = 1000 cells = 20%.

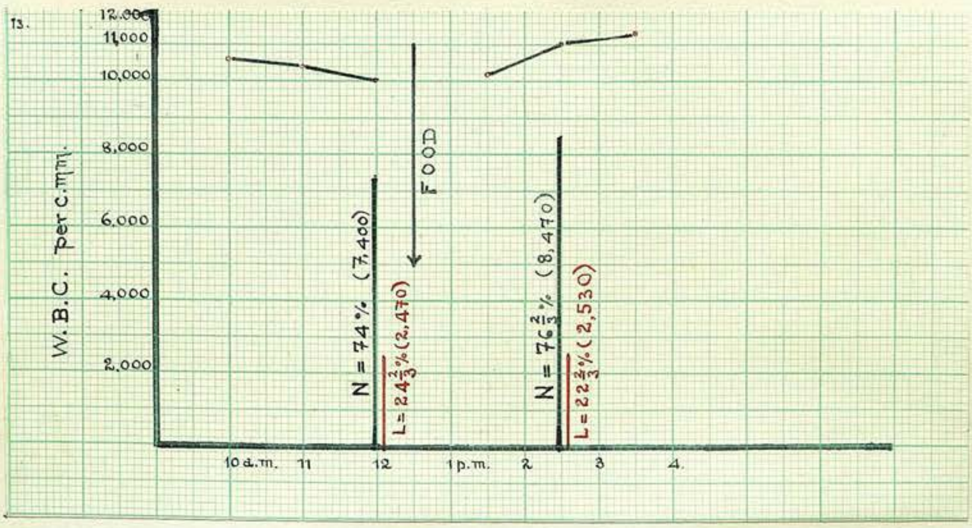
Experiment 13.

Miss R., aet. 20 years, has a slight cold at the time of experiment, but otherwise healthy.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.90% 10,600	
11.0	10,400	
12.0	10,000	B=0.7%; E=0.7%; N=74%; L=24.7% (67) (67) (7400) (2470)
12.30	Full meal.	
1.30 p.m.	Hb.90% 10,200	
2.30	Hb.90% 11,000	B=0%; E=0.7%; N=76.7%; L=22.7% (0) (73) (8470) (2530)
3.30	11,300	



Remarks:

Lowest count at 12.0 a.m. = 10,000 per cmm.
Highest " " 3.30p.m. = 11,300 " "
Difference = 1,300 cells = 13%.

Experiment 14.

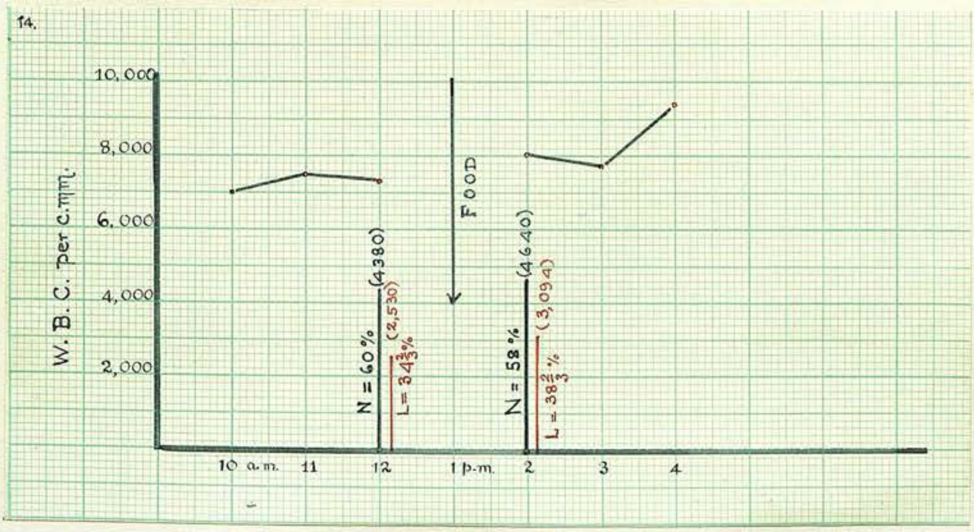
A.D., male aet. 43 years.

Looks healthy, but complains of gastric discomfort. Thought to be early carcinoma of stomach, but subsequent laparatomy proves negative.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.100% 7,000	
11,0	7,500	
12.0	Hb.100% 7,300	B=2.7%; E=2.7%; N=60%; L=34.7% (194) (194) (4380) (2530)
1.0 p.m.	Full meal.	
2.0	Hb.100% 8,000	B=1.3%; E=2%; N=58%; L=38.7% (107) (160) (4640) (3094)
3.0	7,700	
4.0	9,400	



Remarks

Lowest count at 10.0 a.m. = 7,000 per c.mm.
Highest " " 4.0 p.m. = 9,400 " "
Difference = 2,400 cells = 34.3%

Experiment 15.

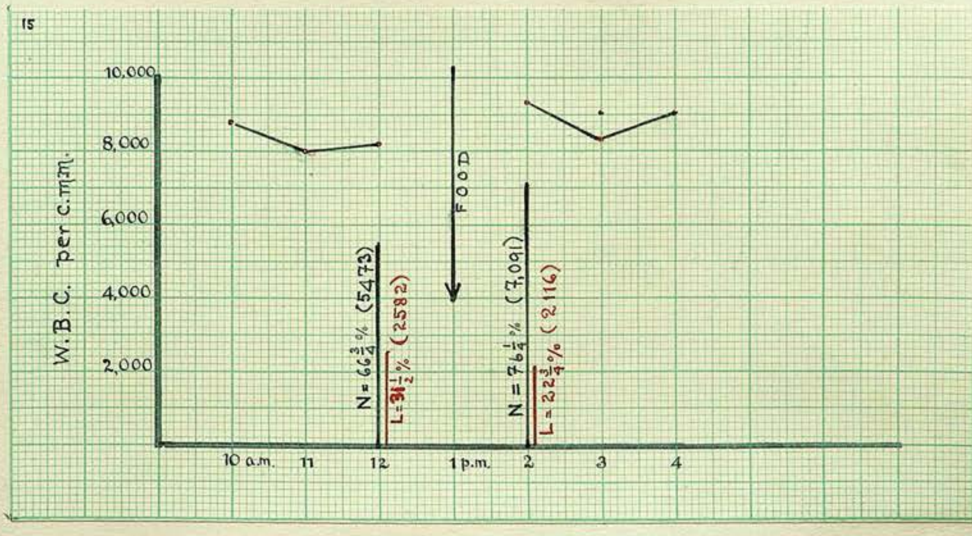
Male, aet. 40 years.

Pneumonia convalescent, 8 days after crisis.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c. per c.mm.	Differential Count.			
10.0 a.m.	8,800				
11.0	Hb.90% 8,000				
12.0	8,200	B=$\frac{3}{4}$%; (61)	E=1%; (82)	N=66$\frac{3}{4}$%; (5473)	L=31$\frac{1}{2}$% (2582)
1.0 p.m.	Full meal.				
2.0	Hb.90% 9,300	B=$\frac{1}{2}$%; (46)	E=$\frac{1}{2}$%; (46)	N=76$\frac{1}{4}$%; (7091)	L=22$\frac{3}{4}$% (2116)
3.0	Hb.90% 8,300				
4.0	9,000				



Remarks:

Lowest count at 11.0 a.m. = 8,000 per c.mm.
Highest " " 2.0 p.m. = 9,300 " "
Difference = 1,300 cells = 16.2% " "

Experiment 16.

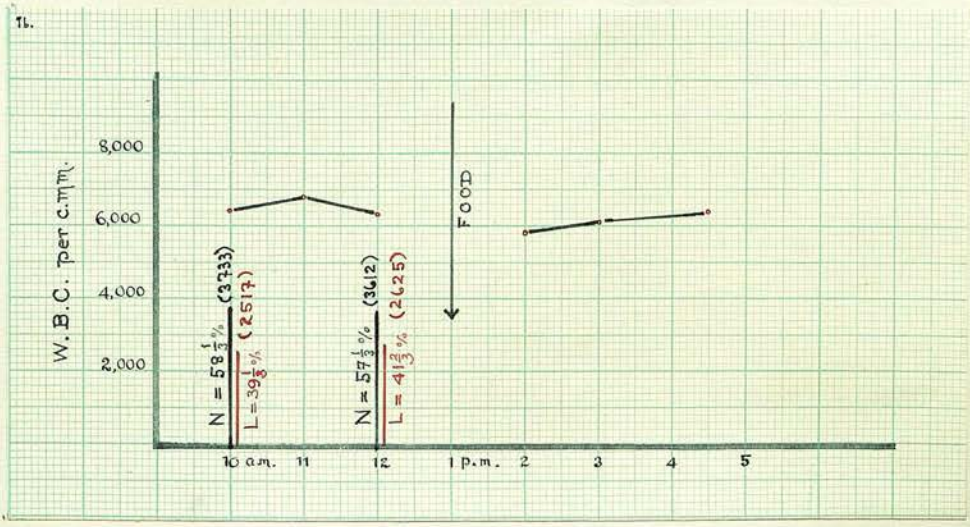
W., male, aet. 28 years.

Had gastric ulcer, but free from symptoms at the time of experiment.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	W.b.c.	Differential Count.
10.0a.m.	6,400	B=0.3%; E=2%; N=58.3%; L=39.3% (21) (128) (3733) (2517)
11.0	Hb.100% 6,800	
12.0	6,300	B=0.3%; E=0.7%; N=57.3%; L=41.7% (21) (42) (3612) (2625)
1.0 p.m.	Full meal.	
2.0	Hb.100% 5,800	
3.0	6,100	
4.30	6,380	



Remarks:

Lowest count at 2.0 p.m. = 5,800 per c.mm.
Highest " " 11.0 a.m. = 6,800 " "
Difference = 1,000 cells = 17.2% " "

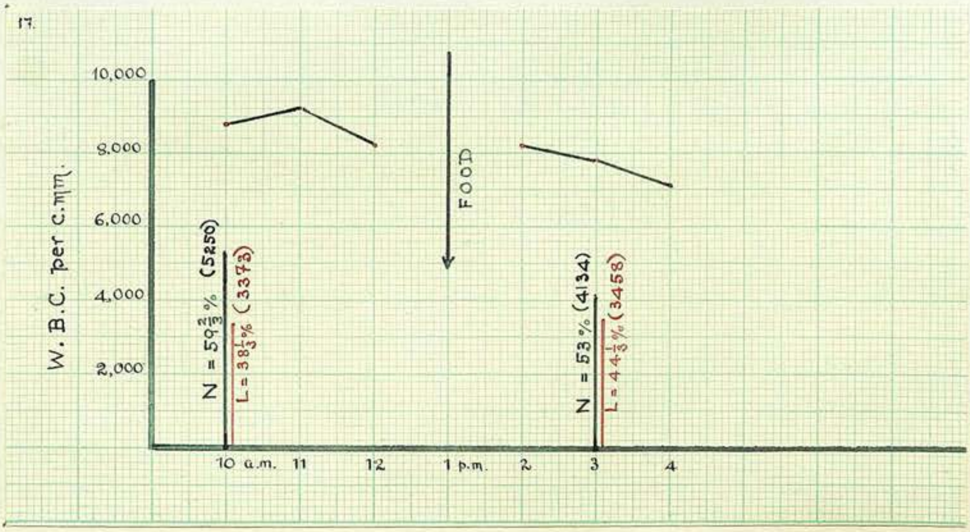
Experiment 17.

J.N., male aet. 26 years, suffering from mild sciatica.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time	w.b.c. per c.mm.	Differential Count
10.0 a.m.	Hb.102% 8,800	B=0%; E=2%; N=59.7%; L=38.3% (0) (176) (5250) (3373)
11.0	9,200	
12.0	8,200	
1.0 p.m.	Full meal.	
2.0	8,200	
3.0	Hb.102% 7,800	B=0.7%; E=2%; N=53%; L=44.3% (52) (156) (4134) (3458)
4.0	7,100	



Remarks:

Lowest count at 4.0 p.m. = 7,100 per c.mm.
Highest " " 11.0 a.m. = 9,200 " "
Difference = 2,100 cells = 30% " "

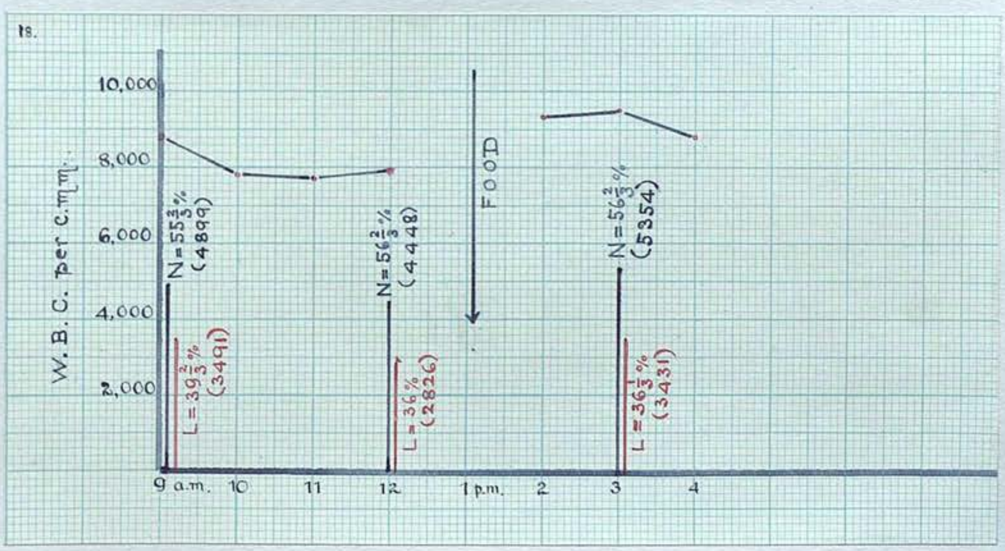
Experiment 18.

J.A., male aet. 36 years, subject of chronic
duodenal ulcer.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
9.0 a.m.	Hb.98% 8,800	B=0.7%; E=4%; N=55.7%; L=39.6% (59) (352) (4899) (3491)
10.0	7,800	
11.0	7,700	
12.0	Hb.98% 7,850	B=1%; E=6.3%; N=56.7%; L=36% (78) (487) (4448) (2826)
1.0 p.m.	Full meal.	
2.0	9,380	
3.0	Hb.98% 9,450	B=0.7%; E=6.3%; N=56.7%; L=36.3% (62) (598) (5354) (3431)
4.0	8,800	



Remarks:

Lowest count at 11.0 a.m. = 7,700 per c.mm.
Highest " " 3.0 p.m. = 9,450 " "
Difference = 1.750 cells = 22.7% " "

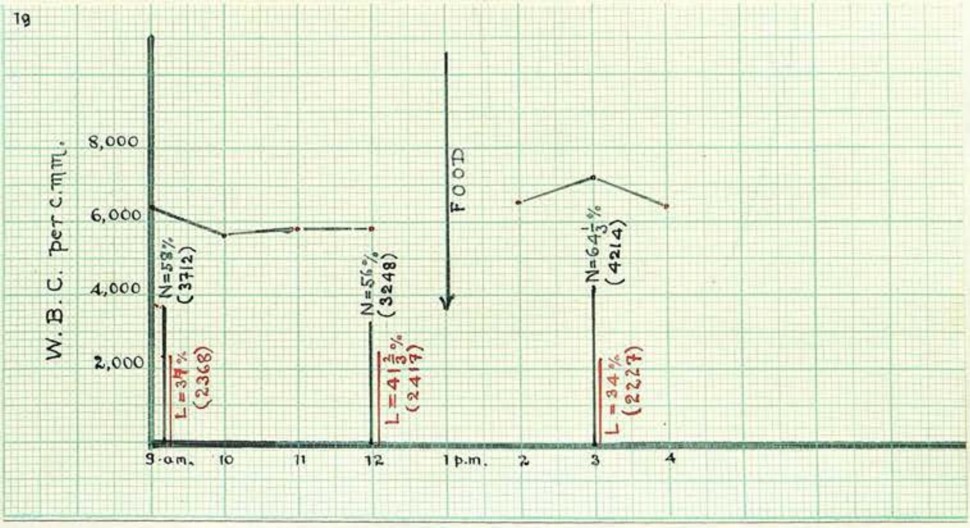
Experiment 19.

L., male aet. 34 years, policeman.
Has complete paralysis of 3rd Nerve.
Otherwise perfectly fit.

Last meal: 7.0 p.m. previous evening.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Counts.
9.0 a.m.	Hb. 100% 6,400	B=1.7%; E=2.3%; N=58%; L=37% (106) (149) (3712) (2368)
10.0	5,600	
11.0	5,800	
12.0	5,800	B=0.7%; E=1.7%; N=56%; L=41.7% (39) (97) (3248) (2417)
1.0 p.m.	Full meal.	
2.0	Hb. 100% 6,550	B=0.7%; E=1%; N=64.3%; L=34% (44) (65) (4214) (2227)
3.0	7,200	
4.0	6,400	



Remarks:

Lowest count at 10.0 a.m. = 5,600 per c.mm.
Highest " " 3.0 p.m. = 7,200 " "
Difference = 1,600 cells = 28.6% " "

G R O U P IIA.

TABLE OF COMPARISON.

No.of Expt.	Lowest Count per c.mm.	Time	Highest Count per c.mm.	Time.	Difference	After mid-day Meal (12.30-1p.m.)
10	6,751	11a.m.	9,350	3p.m.	2600=38.5%	Rise
11	6,700	11a.m.	9,500	1.30p.m.	2800=41.8%	Rise
12	5,000	12a.m.	6,000	11a.m.	1000=20%	No Rise
13	10,000	12a.m	11,300	3.30p.m.	1300=13%	Rise
14	7,000	10a.m.	9,400	4p.m.	2400=34.3%	Rise
15	8,000	11a.m	9,300	2p.m.	1300=16%	Rise
16	5,800	2p.m.	6,800	11a.m	1000=17.2%	No Rise
17	7,100	4p.m.	9,200	11a.m.	2100=30%	No Rise
18	7,700	11a.m.	9,450	3p.m.	1750=22.7%	Rise
19	5,600	10 a.m.	7,200	3p.m.	1600=28.6%	Rise

B. EFFECT OF BREAKFAST.

Conditions of experiment :

Experiments are made on six healthy students at rest, including two subjects employed in GROUP I. A fasting period of approximately twelve hours precedes the breakfast given at 8.55 a.m. Blood count is made shortly before and hourly after the breakfast till noon, except in two cases in which only two counts are made afterwards. On account of the tendency for the number of the leucocytes to rise in the afternoon independent of food, as seen in GROUP I Experiments, no further count is made after 12.0a.m.

The breakfast consists of two fried eggs, three slices of bacon, two large pieces of buttered toast, and two cups of tea.

TABLE OF RESULTS.

Experiment	8.45 a.m.	8.55 a.m.	10.0	11.0	12.0
No. 20 Same subject as in Expt.9	7,500	BREAKFAST	6,600	7,800	7,850
No.21 Same subject as in Expt.4	7,300		7,100	8,400	8,300
No.22	6,500		5,700	6,140	6,300
No. 23	4,900		5,500	5,100	
No. 24	7,800		7,700	8,600	7,500
No. 25	5,940		6,120	7,040	
Expt.	8.45 a.m.	8.55	10.0	11.0	12.0

SUMMARY.

SUB-GROUP A.

(1) Effect of full mid-day meal is tested on ten subjects after a fasting period of about eighteen hours.

(2) There is no increase in leucocytes in 3 cases at the end of three hours after meal (1 healthy person, 1 case of healed gastric ulcer, and 1 case of sciatica).

(3) All the other seven cases show a rise within one to three hours after food, i.e. between 1.30 and 4.0 p.m.

(4) The maximum variation in total leucocytes ranges from 13% to 41.8%, with an average of 26.2%.

(5) In this group the absolute number of the neutrophil polymorphs follows the total white count more closely and constantly than that of the lymphocytes. The maximum alterations in the relative percentage of the neutrophils and lymphocytes are 9½% and 8½%, with average of 5.2% and 4.7% respectively.

(6) The changes in the basophils and eosinophils are variable and slight, averaging less than 0.5% for both.

(7) The haemoglobin remains constant.

(8) The results fall within the normal limit of

variations seen in fasting subject under similar experimental conditions both in regards to time and extent of the rise.

SUB-GROUP B.

Variations after breakfast also fall within fasting limit.

G R O U P III

PATHOLOGICAL CASES.

NO FASTING

Conditions of Experiment:

All the twelve subjects are hospital patients, in ten of whom definite pathological conditions have been diagnosed. They are subject to hospital routine. The first blood examination is made at 10.0 a.m., about two hours after breakfast, and then continued as in Group II. experiments.

Experiment 26.

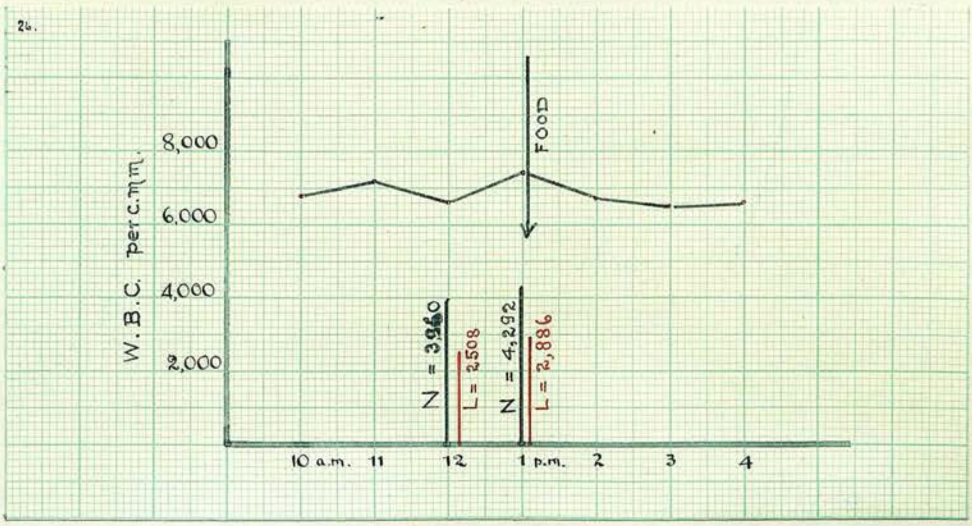
W., male, aet. 40 years.

Complaint: "Giddiness".
Nothing definite was found on examination.

No fasting.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb. 100% 6,800	
11.0	7,200	
12.0	6,600	B=½%; E=1½%; N=60%; L=38% (33) (99) (3960) (2508)
1.0 p.m.	7,400	B=1½%; E=1½%; N=58%; L=39% (111) (111) (4292) (2886)
2.0	Hb. 100% 6,700	
3.0	6,500	
4.0	6,600	



Remarks:

Lowest count at 3.0 p.m. = 6,500 per c.mm.
Highest " " 1.0 p.m. = 7,400 " "
Difference = 900 cells = 14% " "

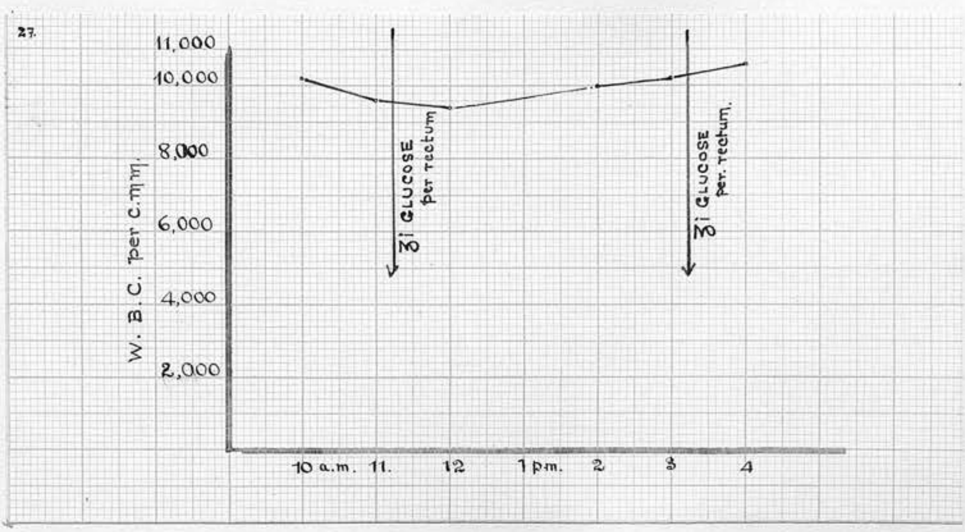
Experiment 27.

J.K., male, aet. 76 years.
Probably a case of malignant growth causing alimentary tract obstruction.

Having glucose saline per rectum four-hourly.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.98%. 10,200	
11.0	9,600	
12.0	9,400	NOT MADE
2.0 p.m.	10,000	
3.0	10,200	
4.0	Hb.98% 10,600	



Remarks:

Lowest count at 12.0 a.m. = 9,400per c.mm.
Highest " " 4.0 p.m. = 10,600 " "
Difference = 1,200 cells = 13.8%

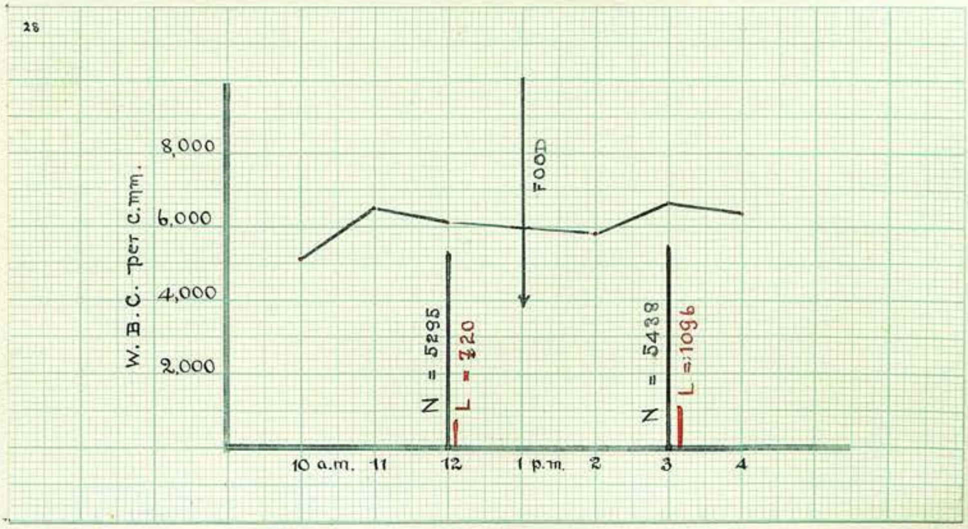
Experiment 28.

J.A., male, aet. 63 years.
Diagnosis: Lymphosarcoma.
Patient died two days later.

No previous fasting.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.90% 5,100	
11.0	6,500	
12.0	6,100	B=0.6%; E=0.8%; N=86.8%; L=11.8% (37) (49) (5259) (720)
2.0 p.m.	Hb.90% 5,800	
3.0	6,600	B=0.4%; E=1%; N=82.4%; L=16.2% (26) (66) (5438) (1069)
4.0	6,300	



Remarks:

Lowest count at 10.0 a.m. = 5,100 per c.mm.
Highest " " 3.0 p.m. = 6,600 " "
Difference = 1,500 cells = 30% " "

The afternoon average is slightly higher than the morning one, but there is no definite increase.

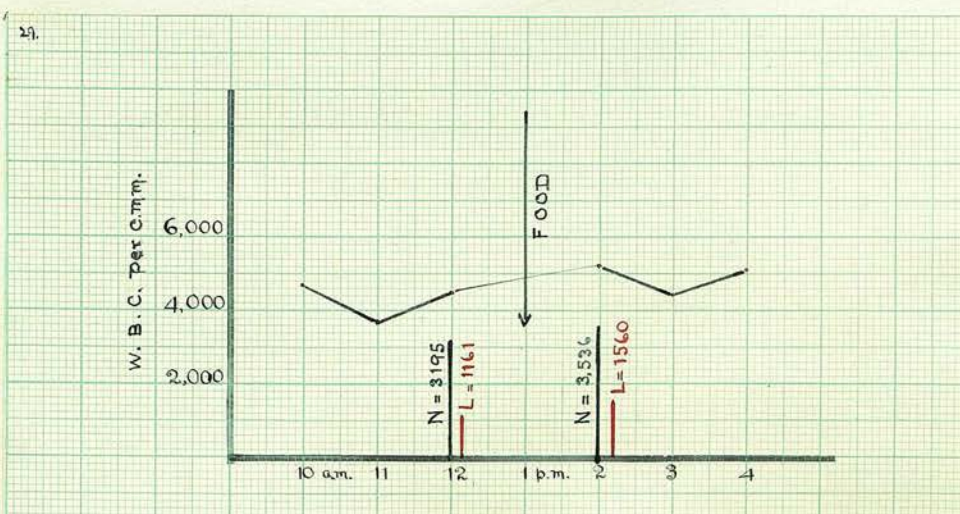
Experiment 29.

J., male, aet 21. years.
Diagnosis: Hodgkin's Disease.
Much improved under X-ray treatment.

No fasting.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb. 69% 4,700	
11.0	3,700	
12.0	4,500	B=0.6%; E=2.6%; N=71%; L=25.8% (27) (117) (3195) (1161)
2.0 p.m.	Hb. 69% 5,200	B=0.6%; E=1.4%; N=68%; L=30%; (31) (73) (3536) (1560)
3.0	4,400	
4.0	5,100	



Remarks:

Lowest count at 11.0 a.m. = 3,700 per c.mm.
Highest " " 2.0 p.m. = 5,200 " "
Difference = 1,500 cells = 40.5%

There is a definite afternoon rise.

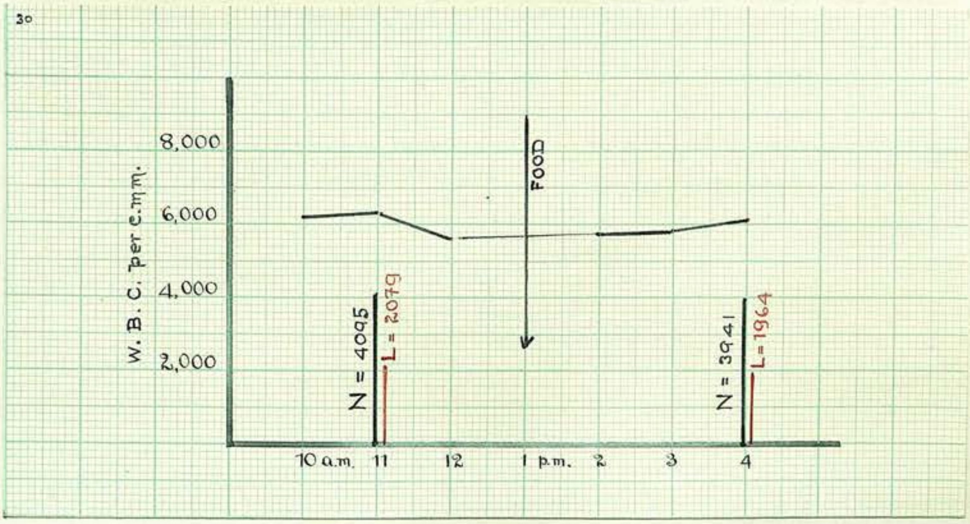
Experiment 30.

F.H., male, aet. 30 years.
Diagnosis: Chronic Pulmonary Tuberculosis. with a small fibrotic cavity in rt. upper lobe, and cervical T.B. glands.

No fasting.

TABLE OF RESULTS

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.86% 6,200	
11.0	6,300	B=0.8%; E=1.2%; N=65%; L=33% (50) (76) (4095) (2079)
12.0	5,600	
2.0 p.m.	Hb.87% 5,700	
3.0	5,800	
4.0	6,100	B=0.6%; E=2.6%; N=64.6%; L=32.2% (37) (158) (3941) (1964)



Remarks:

Lowest count at 12.0 a.m. = 5,600 per c.mm.
Highest " " 11.0 a.m. = 6,300 " "
Difference = 700 cells = 12.5%

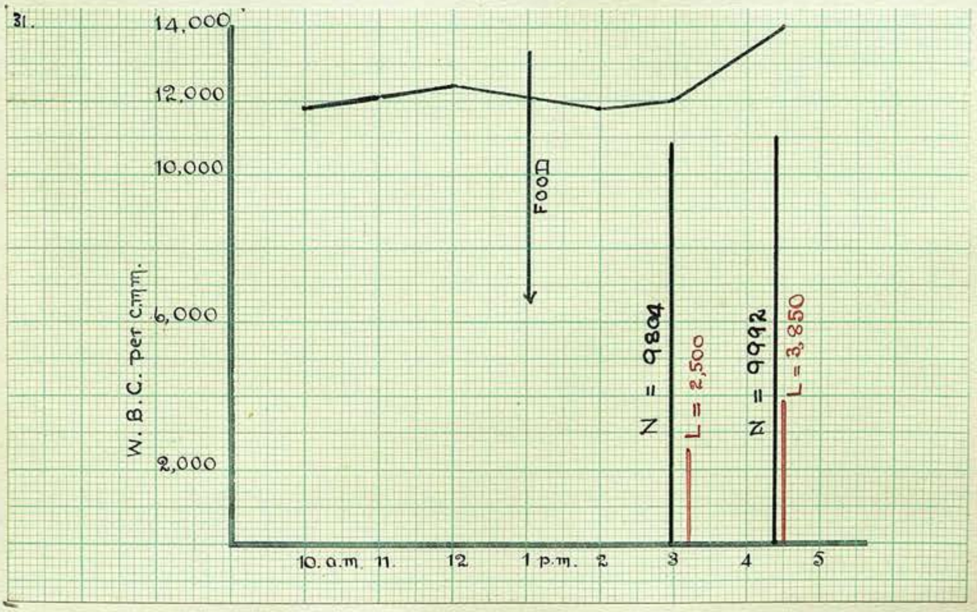
There is no definite rise in the afternoon,

Experiment 31.

J.F., male, aet. 55 years.
Diagnosis: Bronchiectasis.
Evening temperature up to 100°F. but down to normal during the day.
No fasting.

TABLE OF RESULTS.

Time.	W.b.c. per c.mm.	Differential Count.			
10.0 a.m.	Hb.88% 11,800				
11.0	12,000				
12.0	12,400				
2.0 p.m.	11,800				
3.0	Hb.88% 12,000	B=0%; (0)	E=0.8%; (96)	N=78.4%; (9804)	L=20.8% (2500)
4.30	14,000	B=0.2%; (28)	E=1%; (140)	N=71.3%; (9992)	L=27.5% (3850)



Remarks:

Lowest count at 10.0 a.m. &2.0p.m. = 11,800 per cmm.
Highest " " 4.30p.m. = 14,000 "
Difference = 2,200 cells = 18.6% "

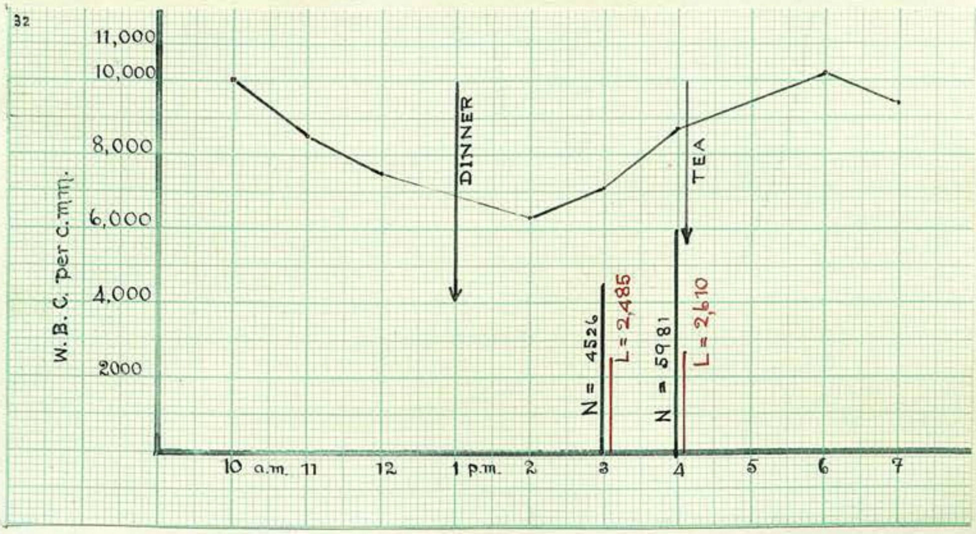
There is a definite increase in the afternoon.

Experiment 32.

H.G.W., male, aet. 30 years.
Diagnosis: Pleurisy with effusion. Temperature not above the normal on the day of the experiment, though previously was up to 101°F.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb. 90% 10,000	
11.0	8,500	
12.0	7,500	
2.0 p.m.	Hb. 90% 6,300	
3.0	7,100	B= $\frac{1}{2}$%; E= $\frac{3}{4}$%; N= 63$\frac{3}{4}$%; L= 35%; (35) (53) (4526) (2485)
4.0	8,700	B= 1%; E= $\frac{1}{4}$%; N= 68$\frac{3}{4}$%; L= 30% (87) (22) (5981) (2610)
6.0	10,200	
7.0	9,400	



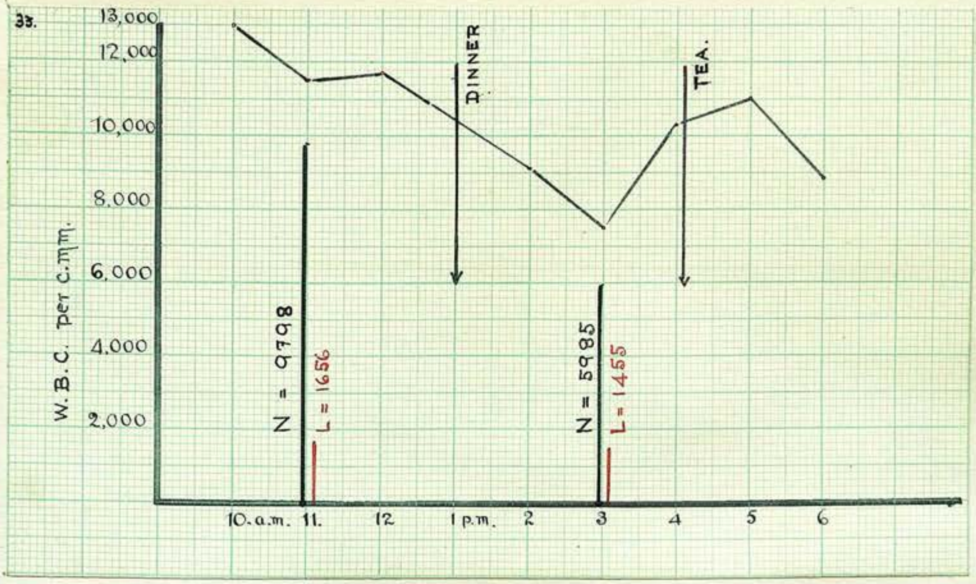
Remarks: Lowest count at 2.0 p.m. = 6,300 per c.mm.
Highest " " 6.0 p.m. = 10,200 " "
Difference = 3,900 cells = 62% " "
A steep fall occurs from morning till early afternoon, followed by an equally steep rise in the late afternoon.

Experiment 33.

W., male, aet. 43 years.
Diagnosis: Apical pneumonia.
First day after temperature has become normal.

TABLE OF RESULTS.

Time.	W.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.92% 13,000	
11.0	11,500	B=0%; E=0.4%; N=85.2%; L=14.4% (0) (46) (9798) (1656)
12.0	11,700	
2.0 p.m.	Hb.92% 9,100	
3.0	7,500	B=0%; E=0.8%; N=79.8%; L=19.4% (0) (60) (5985) (1455)
4.0	10,300	
5.0	11,000	
6.0	8,800	
Following day		
11.0 a.m.	6,000	



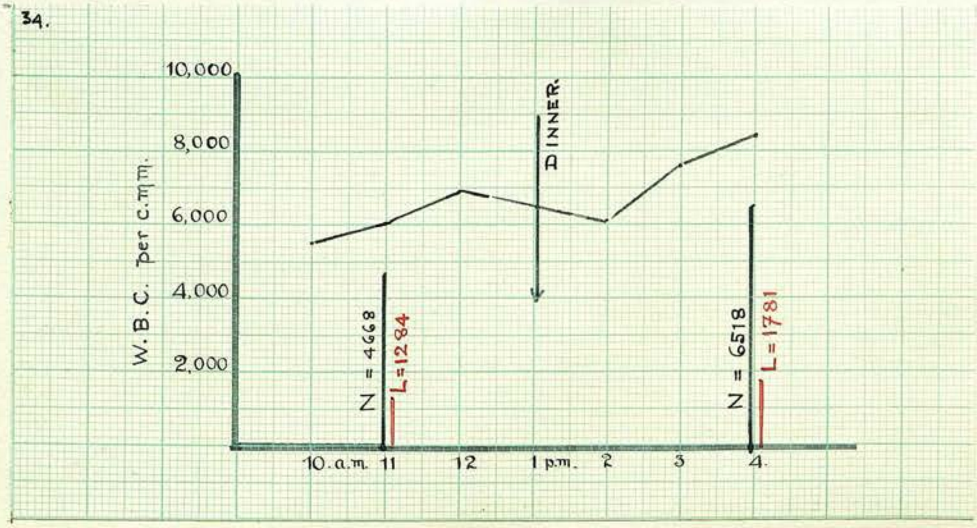
Remarks: The critical fall in the number of leucocytes is interrupted by an afternoon rise of 47%, being highest at 5,0 p.m.

Experiment 34.

R.B., male, aet. 20 years.
Diagnosis: Lobar Pneumonia.
Second day after the crisis.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.87% 5,500	
11.0	6,000	B=0.2%; E=0.6%; N=77.8%; L=21.4% (12) (36) (4668) (1284)
12.0	6,900	
2.0 p.m.	6,100	
3.0	Hb.88% 7,600	
4.0	8,400	B=0.2%; E=1%; N=77.6%; L=21.2% (17) (84) (6518) (1781)



Remarks:

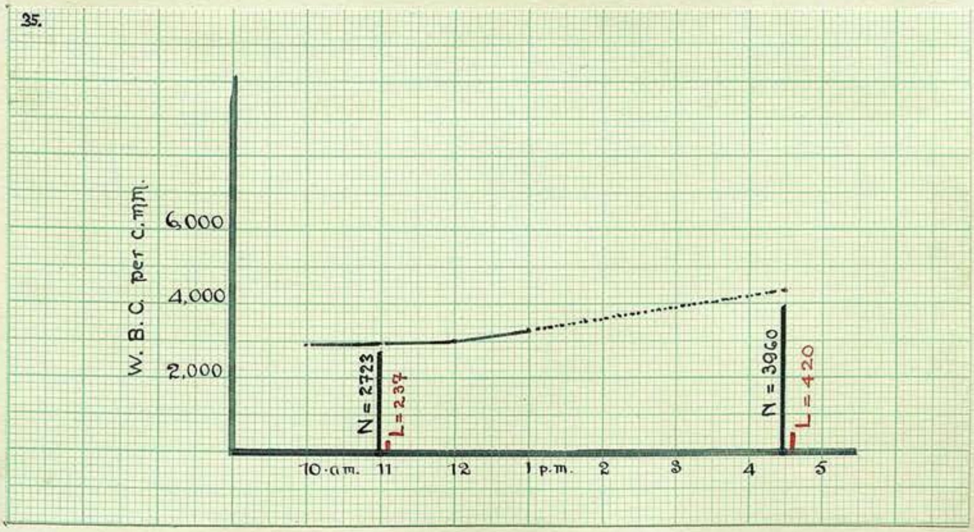
Lowest count at 10.0 a.m. = 5,500 per c.mm.
Highest " " 4.0 p.m. = 8,400 " "
Difference = 2,900 cells = 52.7% " "

Experiment 35.

A.C., male aet. 55 years.
Diagnosis: Pneumonia?
Patient very ill. Temperature 102.5°F.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.86% 2,900	
11.0	2,960	N(incl.Myelocytes) = 92%; L=8% (2723) (237) B & E entirely absent.
12.0	3,000	
1.0.p.m.	3,300	
4.30	Hb.89% 4,380	N(incl. Myelocytes) =90.4%; L=9.6% (3960) (420) B & E entirely absent.



Remarks:

Lowest count at 10.0 a.m. = 2,900 per c.mm.
Highest " " 4.0 p.m. = 4,380 " "
Difference = 1,480 cells = 51% " "

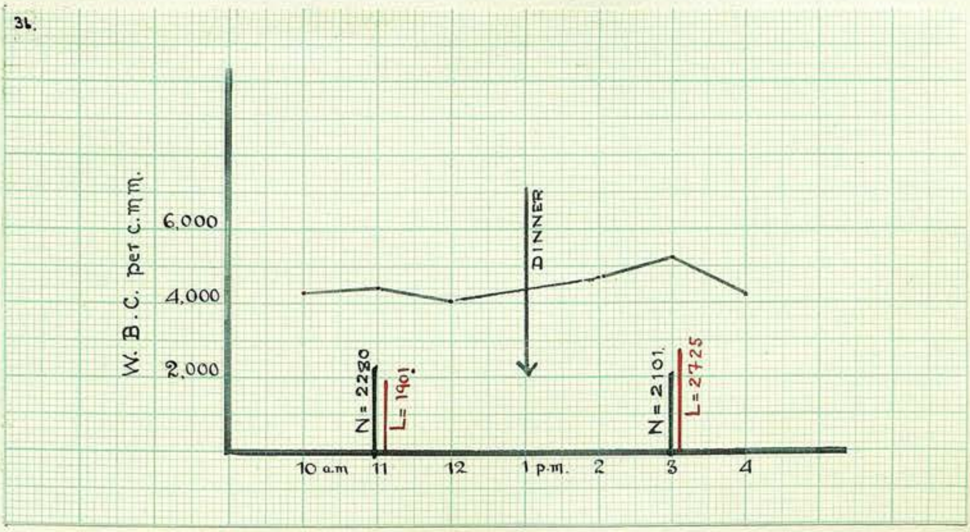
No count was made between 1.0 p.m. and 4.30 p.m., as the patient was too ill to be disturbed.

Experiment 36.

D.Mc., male, aet. 45 years.
Diagnosis: Pernicious anaemia.
Much improved under treatment.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.67% 4,260	
11.0	4,400	B=1.4%; E=3.6%; N=51.8%; L=43.2% (62) (159) (2280) (1901)
12.0	4,000	
2.0 p.m.	Hb.67% 4,700	
3.0	5,200	B=0.4%; E=7%; N=40.4%; L=52.2% (21) (364) (2101) (2725)
4.0	4,200	



Remarks:

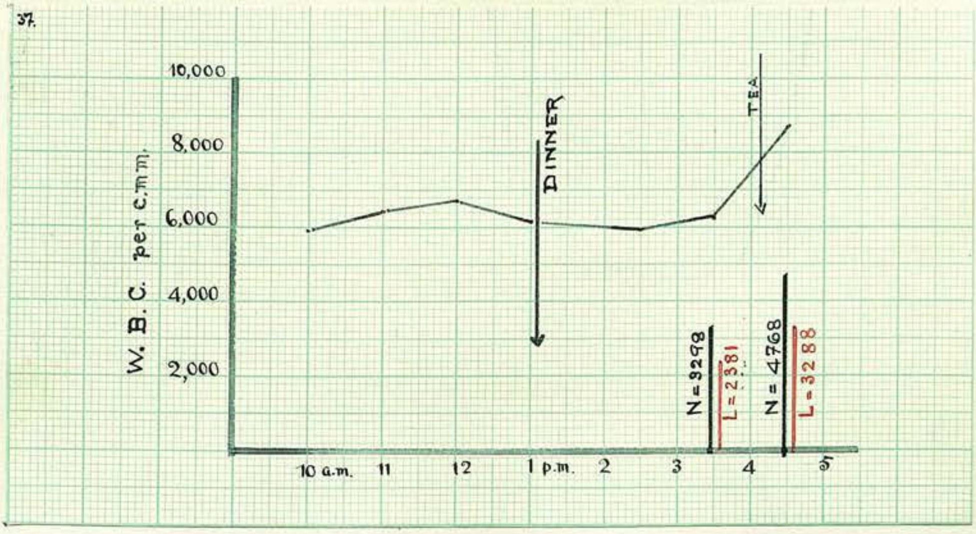
Lowest count at 12.0 a.m. = 4,000 per c.mm.
Highest " " 3.0 p.m. = 5,200 " "
Difference = 1,200 cells = 30%.

Experiment 37.

J.R.B., Male, aet. 47 years.
Diagnosis: Pernicious anaemia.
Much improved under treatment.

TABLE OF RESULTS.

Time.	w.b.c. per c.mm.	Differential Count.
10.0 a.m.	Hb.78% 5,920	
11.0	6,400	
12.0	6,700	
1.0 p.m.	6,140	
2.30	5,940	
3.30	Hb.78% 6,200	B=1.4%; E=7%; N=53.2%; L=38.4% (87) (434) (3298) (2381)
4.30	8,700	B=1.8%; E=5.6%; N=54.8%; L=37.8% (157) (487) (4768) (3288)



Remarks:

Lowest count at 10.0 a.m. = 5,920 per c.mm.
Highest " " 4.30p.m. = 8,700 " "
Difference = 2780 cells = 47% " "

GROUP III.

TABLE OF COMPARISON.

No. of Expt.	Lowest count per c.mm.	Time	Highest Count per c.mm.	Time	Difference	After-noon rise
26	6,500	3p.m.	7,400	1.p.m.	900= 14%	Yes
27	9,400	12a.m.	10,600	4p.m.	1200= 13.8%	Yes
28	5,100	10a.m.	6,600	3p.m.	1500= 30%	Not definite
29	3,700	11a.m.	5,200	2p.m.	1500= 40.5%	Yes
30	5,600	12a.m.	6,300	11a.m.	700= 12.5%	No
31	11,800	10a.m.	14,000	4.30p.m.	2200= 18.6%	Yes
32	6,300	2p.m.	10,200	6p.m.	3900= 62%	Yes
34	5,500	10a.m.	8,400	4p.m.	2900= 52.7%	Yes
35	2,900	10a.m.	4,380	4.30p.m.	1480= 51%	Yes
36	4,000	12a.m.	5,200	3p.m.	1200= 30%	Yes
37	5,920	10a.m.	8,700	4.30p.m.	2780= 47%	Yes

N.B. Case of pneumonial crisis is omitted from the table.

SUMMARY.

(1) Serial white counts are made on 12 pathological cases without any fasting.

(2) 2 cases show no afternoon increase, namely,

1. Chronic Pulmonary Tuberculosis with enlarged cervical glands.
2. Lymphosarcoma (2 days before death).

(3) Following 10 cases exhibit afternoon rise of varying degrees:-

3 Leucopaenic Cases:
1. Pernicious anaemia.
2. Hodgkin's Disease (slightly leucopaenic after prolonged X-ray therapy).
3. An acute febrile case with failure of leucocytic reaction (Pneumonia?), death occurring the following day.

3 cases with about normal number of leucocytes:
4. Case of uncertain aetiology.
5. Pernicious anaemia.
6. Lobar Pneumonia, two days after crisis.

4 cases with slight leucocytosis:
7. Alimentary obstruction, probably malignant.
8. Bronchiectasis.
9. Apical Pneumonia, first day after crisis.
10. Pleural effusion.

(4) Except in Expt. 33, in which the rise interrupts the fall following crisis of pneumonia, the maximum variation ranges from 13.8% to 62%, with average of 33.8%.

(5) Except in Expt. 36, in which the increase is due to lymphocytes and eosinophils only, the absolute numbers of neutrophil polymorphs and of lymphocytes rise with the total leucocytes. No absolute constancy is found regarding alteration

in relative percentage, the maximum variation being 11.4% for the neutrophils and 9% for the lymphocytes, with average of 3.5% and 3.2% respectively.

(6) Basophils and eosinophils show inconstant and insignificant change, except in one case of Pernicious Anaemia, in which an eosinophil increase of 3.4% or 205 cells per c.m.m. is noted.

(7) There is a definite blood concentration in only one case (Expt. 35) as a result of perspiration; haemoglobin rises by 3%, but the leucocytes show an increase of 51%.

DISCUSSION

Since the publication of Sabin's work the occurrence of afternoon rise in the number of leucocytes in man has been confirmed by many observers. While all of these unanimously agree that the rise occurs regardless of food, many theories have been put forward to account for the phenomenon, and these have already been referred to in the summary of literature. Since one object of this investigation is to test the effect of food on the number of leucocytes, it will perhaps not be out of place to touch upon this aspect of the question again on the basis of personal observations. The conclusion arrived at in this work regarding digestion is that it has no appreciable effect on the number of white blood cells in the peripheral blood of man. There is no evidence that food superimposes its effect on the normal afternoon rise, for the results of different experiments which were carried out on the same individuals on different days which were far apart did not show any essential difference as regards time of day and extent of the rise whether food was given or not, although the figures obtained were not absolutely identical. The number of such experiments is too small, however, to permit of such a conclusion as was arrived at by Smith and Mc.Dowell[11], who record only a few cases, that there is a characteristic pattern of variations for each individual. It may be admitted here that, had control experiments not been carried out on fasting persons, the food and the post-meridian rise might have been easily and erroneously considered as cause and effect, on the presupposition that there is no significant variation during period of fasting. It is not surprising to see great variability recorded by earlier observers regarding the time that elapses after meal before a definite rise begins and reaches its height; for if food is administered earlier in the day, it will probably take many hours before the rise occurs, but if it is given at noon or in the early afternoon, the increase in the number of the leucocytes will soon become evident. The degree of increase observed in fasting persons in this work compares closely with that attributed to the effect of food by the supporters of digestion leucocytosis in man. Their failure cases were probably the type of cases which would fail to show any afternoon rise; such cases are in the minority. Is it possible that this post-meridian rise may have been primarily due to the habit of the bone marrow to liberate more cells into the circulation in connection with the chief meal of the day, and that this habit is still manifest even when food is withheld, in other words, a conditioned reflex has been established? The failure of a big mixed meal, even when taken at the usual time, to produce any increase in the number of white cells in some normal persons, who have previously fasted for at least sixteen hours, renders the reflex hypothesis untenable.

The results recorded in Group III indicate that even in cases with organic lesions there is still a tendency for the leucocytes to increase in the afternoon, although in a few cases the rise begins a little later than is usually found in normal persons. The phenomenon is observed in leucopaenic as well as in cases with leucocytosis. It is remarkable that in two cases of pulmonary inflammatory condition, subacute at the time, the rise occurs after a progressive and considerable fall, which begins in the morning and reaches its depth about the middle of the afternoon; the rise in one of these cases, though quite conspicuous, never reaches the morning highest count, but it is almost certain that the progressive fall before the rise in this case is due to the natural lowering of the level of the number of leucocytes following pneumonial crisis and the count made at 11.0 a.m. the following day confirms this. The post-meridian rise in Expt. 35 is quite definite, and obviously not entirely due to concentration of the blood, although the patient was acutely ill, with marked failure of leucocytic reaction. How much of the rise found in this last group of cases is influenced by the underlying pathological process, and how much is due to the normal tendency as seen in healthy persons, is difficult to say. Nevertheless, it is interesting to note the similarity of the results obtained in different groups of experiments.

It has been noted in some cases in all groups that the leucocyte number is not always lowest during rest, and that it may even show an increase during the afternoon nap.

Light, effortless movement of the body does not appear to increase the leucocyte count. This opinion is based on a few preliminary experiments on normal persons. It was also noted in one case in the ward that there was no leucocyte increase just after he had finished washing himself in bed. It appears, therefore, that mental activity and physical exertion cannot be factors responsible for the so-called afternoon rise observed in this work. It would be interesting to know if this oft observed phenomenon bears any relation to some cyclical event in the body of man.

Large fluctuations in the total count as recorded by Sabin[9)] and Smith and Mc.Dowell[11)] have not been observed in this investigation, although smaller ones of generally not exceeding ± 1000 cells per c.mm. have frequently been noted. These large fluctuations found by the above observers seem to be due to a relatively higher percentage of error due to not counting sufficiently large number of white cells; this fact has been well demonstrated by Ponder[14)], and is confirmed by my own observations.

CONCLUSIONS.

(1) Both in normal and pathological states the leucocytes of man frequently, but not invariably, show an increase in the afternoon.

(2) This increase occurs regardless of food and rest, and averages about 31%.

(3) The variations in the number of leucocytes observed even after a full mixed meal fall within the limit found in normal fasting persons under similar experimental conditions.

(4) No absolute constancy is found regarding the change in the relative percentage of the various cell types, but this is small on the average. In most cases the absolute numbers of the neutrophil polymorphs and lymphocytes rise and fall with the total white cells. The changes affecting the numbers of the basophils and eosinophils are variable and generally slight, although in a few cases the eosinophils show a variation of about 3%. Owing to the relatively small number of them being counted, the percentage of error is probably great.

(5) Fluctuations of about ± 500-1000 cells per c.mm. of leucocytes may occur during the day, apart from a definite rise or fall in the total count, but no definite regularity has been observed. These small fluctuations still persist even after

a sufficient margin of error has been allowed for.

(6) The haemoglobin remains practically constant during the day.

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ACKNOWLEDGMENTS.

I wish to express my deep gratitude to Dr. Alexander Goodall for his kind suggestions and permission to carry out experiments on some of the patients under his care. I also wish to express my appreciation to Sister Grant, of Ward 31, Royal Infirmary, Edinburgh, for arrangements made in connection with certain of the experiments. To all the ladies and gentlemen who submitted themselves for experiments carried out outside the hospital my thanks are also due.
